Infective endocarditis due to *Neisseria meningitidis*: two case reports

J. Benes[1,], O. Dzupova[1], M. Kabelkova[1], P. Krizova[2] and A. Gabrielova[3]*

[1]Department of Infectious Diseases, 3rd Faculty of Medicine, Bulovka University Hospital, Budinova 2, 180 81 Prague, [2]National Reference Laboratory for Meningococcal Infections and National Meningococci Surveillance Center, National Institute of Public Health, Prague and [3]Department of Clinical Microbiology, Bulovka University Hospital, Prague, Czech Republic

[*]Tel/Fax: +420 2 6608 2707 E-mail: benesj@cesnet.cz

Two cases of meningococcal endocarditis are described. An 84-year-old man developed sepsis and septic shock and died 15 h after admission to the department. The autopsy revealed aortic endocarditis. Blood and vegetation culture yielded *Neisseria meningitidis* B:16:P1.5. A 37-year-old man was admitted for fever and rash lasting several weeks. Endocarditis of the bicuspid aortic valve caused by *N. meningitidis* C:2a:P1.2,5 was found. The patient was successfully treated with penicillin G for 4 weeks. Brief epidemiologic characteristics of invasive meningococcal disease in the Czech Republic are given.

Keywords Infective endocarditis, *N. meningitidis*, bicuspid aortic valve

Accepted 28 January 2002

Clin Microbiol Infect 2003; 9: 1062–1064

Neisseria meningitidis is commonly known as the agent responsible for acute sepsis and purulent meningitis. Nonetheless, it may also cause persistent bacteremia without signs of sepsis, nonhemorrhagic rash, arthritis, pericarditis, cranial nerve palsy, urinary tract infection or pneumonia [1].

The incidence of *N. meningitidis* endocarditis—like that of *N. gonorrhoeae* endocarditis—was higher in the pre-antibiotic era [2]. Nowadays, it is very rare: for the past 10 years, we found only five case reports in literature (Medline database) [3–7]. We report two cases of meningococcal endocarditis that occurred in our department during the past 10 years.

Case 1: an 84-year-old man was suffering from fever reaching 38.7 °C, anorexia, and weakness; the symptoms lasted for 8 days. Two days prior to admission, he developed dyspnea and repeated vomiting immediately upon the intake of food or fluids. His personal medical history included pancreatitis 15 years previously, bilateral pneumonia, and a minor stroke 2 years previously. He was taking digoxin, pentoxyphyllin and nitrates for his coronary heart disease and angina. He had not traveled before the onset of the disease.

On admission, the patient was lucid, tired, dehydrated and dyspneic. He complained of anorexia and vertigo. Auscultation of the lungs revealed no abnormality. A systolic murmur of moderate intensity was present over the heart, with a maximum in the left parasternal region. Blood pressure was 80/50 mmHg, pulse 86/min, and respiratory rate 30/min. The liver was enlarged to 2 cm below the costal margin. No rashes were present in the skin. Meningeal signs were negative.

Laboratory tests gave the following results: blood glucose 10.3 mmol/L; urea 22.4 mmol/L; creatinine 312 μmol/L; sodium 131 mmol/L; potassium 4.5 mmol/L; chloride 89 mmol/L; white blood cell count 30×10^9/L; hemoglobin 138 g/L; and platelet count 210×10^9/L. The erythrocyte sedimentation rate (ESR) was 76 mm/h. The electrocardiogram (ECG) showed sinus rhythm with signs of left ventricular overload.

The patient was given intensive care, including parenteral rehydration, continuous catecholamine administration and mechanical ventilation. Nevertheless, the circulatory failure was irreversible, and the patient died 15 h after admission.

The autopsy showed a cauliflower-like vegetation of 2 × 1 cm on the anterior cusp of the aortic valve. The involved cusp was perforated, and histologic examination revealed an inflammatory infiltrate reaching into the myocardium. The whole valve showed degenerative changes (foci of dystrophy, calcification). Gram stain examination of specimens was inconclusive. Concomitant findings included septic activation of the spleen (weight: 190 g), a septic thrombus in one of the small brain arteries, bilateral pulmonary edema, brain edema, and gastric ulcer. The patient also had generalized atherosclerosis of the 3rd degree and prostatic hypertrophy.

N. meningitidis B:16:P1.5 grew in a blood culture collected after admission. The same strain was isolated from the vegetation after post-mortem examination of the heart valve.

Case 2: a 37-year-old man with an unremarkable personal medical history had suffered from low-grade fever, fatigue, headache, sore throat and arthralgia for 2 weeks. The ESR at that time was 17 mm/h. The patient was treated with antipyretics only. The illness was followed by fatigue and intermittent chest pain.

Intermittent febrile episodes up to 40 °C began 6 weeks later, together with severe arthralgia, exhaustion, chills and profuse sweating. A generalized maculopapular rash appeared 7 days later. It was especially apparent on the extremities and the abdomen. The efflorescences were pink to livid, sometimes remaining visible for several days, and sometimes disappearing within a few hours. Around the joints, the rash was often associated with local edema and skin hypersensitivity. The patient's overall state remained good, and therefore his general practitioner prescribed antipyretics only.

When the illness did not resolve in 3 weeks, routine laboratory tests were performed, and gave the following results: ESR 102 mm/h; white blood count 10.6×10^9/L (76% polynuclear neutrophils, 21% lymphocytes, 3% monocytes); and hemoglobin 126 g/L. The level of C-reactive protein (CRP) was markedly elevated according to a semiquantitative test. Other tests (liver function, blood glucose, urinalysis, chest X-ray, throat swab) did not show any pathology. The patient was referred to our department for a fever and rash of unknown origin.

On admission, the patient was tired, lucid, of good nutritional status, and febrile (39.3 °C). He complained of a mild headache. His throat was slightly swollen and reddened. Clinical (physical) examination of chest and abdominal organs did not reveal any pathological fundings (affection). Blood pressure was 120/80 mmHg, heart rate 120/min, and respiratory rate 20/min. Meningeal signs were negative. A pink maculopapular rash was present all over the patient's body.

Tests and examinations performed at our department were compatible with a severe bacterial infection without alteration of coagulation parameters: white blood cell count 16.4×10^9/L (74% granulocytes, 8% band forms, 4% monocytes, 14% lymphocytes); platelet count 516×10^9/L; activated partial thrombin time 32.5 s; international normalized rate 1.14; coagulation 80 s; fibrinogen 6.9 g/L; albumin 29 g/L; IgG 15.2 g/L; IgA 4.8 g/L; IgM 1.6 g/L. The anti-streptolysin O titer was within the normal range; syphilis test (VDRL), rheumatoid factor test and serum autoantibodies (anti-ds-DNA, ANA) were negative; the ECG showed no signs of arrhythmia or ischemia.

After 2 days of hospitalization, a new systolic murmur was heard in the 3rd intercostal area. Transesophageal echocardiography (TEE) showed a bicuspid aortic valve with a vegetation of 3–4 mm at the right commissure (Fig. 1). Once blood cultures were collected, treatment with cefalothin was initiated at a dose of 2 g every 4 h. The patient responded to the antibiotic therapy with a lytic decrease of temperature, paling of the rash, and disappearance of all symptoms.

All of the five collected blood cultures yielded *N. meningitidis* C:2a:P1.2,5, sensitive to penicillin,

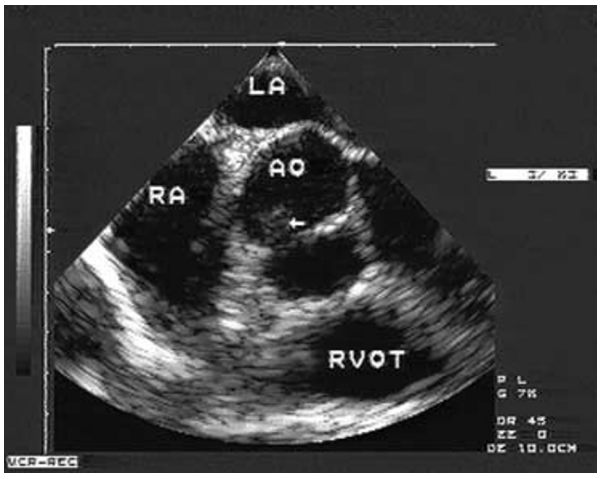

Figure 1 Patient no. 2: a vegetation of 3–4 mm in the right commissure of the bicuspid aortic valve.

cefalothin, chloramphenicol, erythromycin, tetracycline, and gentamicin. On the basis of these findings, treatment was changed to penicillin, 5 million Units every 6 h. The minimal inhibitory concentration (MIC) for penicillin was 0.047 mg/L, that for ampicillin was 0.064 mg/L, and that for cefalothin was 0.25 mg/L.

Treatment with penicillin lasted for 4 weeks overall. The patient remained apyretic and asymptomatic throughout. Check TEE revealed only a slight residual echodensity at the site of the previous vegetation; valvular function was normal. Upon discharge, the patient showed no signs of relapse during the ensuing 6 months.

Both of the cases reported here fulfill the Duke criteria for definite endocarditis [8]. The course of the disease was substantially different in the two patients. The first case involved a fulminant disease progressing to multi-organ failure and death. The second patient developed a subacute illness, with fever and rash as the main symptoms. Neither of the patients developed meningitis or hemorrhagic exanthema. The absence of meningitis corresponds with other reports of meningococcal endocarditis: meningitis did not accompany endocarditis, not even in cases where symptoms lasted for several weeks [6,7,9].

Serotype 16 of *N. meningitidis* B is rare in the Czech Republic. According to data from the National Meningococci Surveillance Center, it was found in only nine of the total of 1336 serogroup B strains collected during the period 1973–2001. Phenotype B:16:P1.5 was found only in the case of endocarditis presented here.

Endocarditis in the second case was caused by *N. meningitidis* C:2a:P1.2,5. Meningococcal strains of this phenotype belong to the hypervirulent complex ET-15/37, ST-11. These strains have spread in the Czech Republic since 1993 and caused an increase in the morbidity of invasive meningococcal disease. The fatality rate in these cases has reached 20%, while the average fatality rate of invasive meningococcal disease before 1993 was 3–5% [10,11].

In most case reports, meningococci isolated from endocarditis patients were established only at the species level. Only three strains of meningococci were further subtyped. They were *N. meningitidis* serogroup B [12], *N. meningitidis* serogroup C [4], and *N. meningitidis* serogroup Y [6]. The more detailed subtyping has not been presented in any of the cases. To our best knowledge, we report the first cases of meningococcal endocarditis in which the detailed characterization of the bacteria is given.

REFERENCES

1. Apicella MA. *Neisseria meningitidis*. In: Mandell GL, Bennett JE, Dolin R, eds. *Principle and practice of infectious diseases*. Philadelphia: Churchill Livingstone, 2000: 2228–41.
2. Firestone GM. Meningococcus endocarditis. *Am J Med Sci* 1946; 211: 556–64.
3. Joao I, Marques P, Namora J *et al. Neisseria meningitidis* native valve endocarditis. A case report. *Rev Port Cardiol* 2001; 20: 877–80.
4. Candrick J, Segasothy M, Wheaton G, Rajabalendran N, Morey F. Meningococcal endocarditis in a patient with rheumatic heart disease. *Aust NZ J Med* 1999; 29: 749–50.
5. Venogopalan P, Alexander PC, Aithala G, Koul RL, Shenoy AK. A child with *Neisseria meningitidis* endocarditis and *Staphylococcus aureus* septicaemia. *J Trop Dis* 1999; 45: 360–1.
6. Lin H, Parekh RS, McQuillan MA, Braun DK, Markovitz DM. Meningococcal endocarditis presenting as cellulitis. *Clin Infect Dis* 1995; 21: 1023–5.
7. Gunn J, Gaw A, Trueman AM. A case of meningococcal endocarditis. *Eur Heart J* 1992; 13: 1004–5.
8. Durack DT, Lukes AS, Bright DK, the Duke Endocarditis Service. New criteria for diagnosis of infective endocarditis: utilisation of specific echocardiographic findings. *Am J Med* 1994; 96: 200–9.
9. Dennis J, Edwards LD, Fisher TN, Makeever L. Endocarditis on a Björk–Shiley mitral prosthesis due to *Neisseria meningitidis*. *Scand J Thorac Cardiovasc Surg* 1977; 11: 205–9.
10. Kriz P, Musilek M. Changing epidemiology of meningococcal invasive disease in the Czech Republic caused by a new clone *Neisseria meningitidis* C:2a:P1.2(P1.5), ET-15/37. *Cent Eur J Public Health* 1995; 3: 189–94.
11. Kriz P, Vlckova J, Bobak M. Targeted vaccination with meningococcal polysaccharide vaccine in one district of the Czech Republic. *Epidemiol Infect* 1995; 115: 411–18.
12. Weetman AP, Matthews N, O'Hara SP, Amos N, Williams BD, Thomas JP. Meningococcal endocarditis with profound acquired hypocomplementaemia. *J Infect* 1985; 10: 51–6.